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Masks and Respirators for Prevention of Respiratory Infections: A State of the Science Review

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Corresponding author:

Trisha Greenhalgh

trish.greenhalgh@phc.ox.ac.uk

Author Affiliation:

University of Oxford.

Greenhalgh, T¹; Baker, M²; Bhattacharjee, S³; Chughtai, AA⁴; Fisman, D⁵; Kunasekaran, M⁶; Kvalsvig, A⁷; Lupton, D⁸; Macintyre, CR⁹; Oliver Meng, M¹⁰; Tawfiq, E¹¹; Ungrin, M¹²; Vipond, J¹³.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 January 2024 and was last updated on 19 January 2024.

INTRODUCTION

Review question / Objective This review has three main objectives. First, to summarise the evidence base from multiple disciplines and study designs for the benefits—and also the practicalities, disbenefits and harms—of masks and masking. Second, to examine why the evidence on these topics is so widely misunderstood, misinterpreted or dismissed. And third, to outline an agenda for future research.

The review questions are:

1. What is evidence from experimental and observational studies for the efficacy and safety of masks and respirators in healthcare and community settings?
2. What is evidence from mechanistic studies (e.g. basic science, social and psychological studies, policy studies) to explain how and why masks and respirators work and why they may not work in some settings?

Rationale The need for a new review on masks was highlighted by a polarization in scientific opinion. The masks section of a 2023 Cochrane review of non-pharmaceutical interventions was—controversially—limited to randomised controlled trials (RCTs). It was interpreted by the press and by some but not all of its own authors to mean that “masks don’t work”. Some scholars questioned the review’s methodology, suggesting that there were key flaws in the meta-analysis and that a vast body of non-RCT evidence had been omitted, distorting the findings and producing a misleading conclusion.

There are additional sources of confusion which this review seeks to clarify. The term ‘mask’ covers a multitude of devices with different material properties; respirators have a more standardised design but are not widely used even in healthcare settings. Some clinical trials of masks and respirators did not adequately define or optimize the intervention or maintain its fidelity, used heterogenous interventions and outcomes, or

failed to measure whether masks were actually worn. In non-RCT studies, it is hard to isolate the effect of masking from that of confounding, effect modification and bias, such as use of other mitigations, concurrent lockdown or changes in disease prevalence. Mask mandates, which require everyone to wear a mask in certain circumstances, have played out differently in different jurisdictions and socio-cultural settings. Masks are not just protective devices; they are cultural and even political symbols about which people feel strongly. Misinformation about masks is widely circulated.

Masking and support for it have declined since the peak of the COVID-19 pandemic, raising societal and ethical questions about whether and for how long the healthy majority should compromise their 'freedom' to help protect the clinically vulnerable (for whom a COVID-19 infection could be life-threatening) and prevent the long-term sequelae of the condition. Masking of healthcare workers has become a management-versus-unions issue, especially in relation to whether and when more costly respirator-grade respiratory protection is needed. Nosocomial COVID-19 is widespread and carries significant mortality, though few healthcare facilities measure or report on its incidence. Aged care facilities are beset with COVID-19 outbreaks. Whatever their protective effects, masks have some drawbacks and some people find it difficult or impossible to wear them. Disposable masks and respirators contribute to non-biodegradable waste and environmental pollution. Research on recycling, reuse and novel materials points to some potential solutions.

Part of the confusion around this topic can be traced back to philosophical issues such as ontology (what is the nature of reality?) and epistemology (how can we know that reality?). Different scholars took widely differing views on these issues. The Cochrane review of non-pharmaceutical interventions, for example, rests on an assumption that the only evidence, whatever the field and research question, must come from RCTs, and that non-RCT evidence is irrelevant. An alternative view is that evidence-based medicine's (EBM's) 'hierarchy of evidence' (with RCTs as the assumed stand-alone gold standard) is inappropriate for a topic as multifaceted as masking. Some have argued that the scientific value of the RCT has become inflated, particularly among doctors, leading them to overlook high-quality non-RCT evidence (for example, mechanistic evidence about how the virus spreads, which can inform optimization of intervention design, or studies of how masking policies played out in the real world) and allowing poor-quality RCTs (for example, of interventions which do not take account of mechanism and

which may therefore mislead rather than inform) to be published in high-impact journals and gain undue influence.

This review sought to review the totality of evidence, including a much-needed reanalysis of the primary studies addressed in the controversial Cochrane review.

Condition being studied This review seeks to summarise the evidence base from multiple disciplines including public health, epidemiology, infectious diseases, biosecurity, fluid dynamics, materials science, modelling, data science, sociology, anthropology, psychology, occupational hygiene on the benefits—and also the practicalities, disbenefits, harms and personal and sociocultural impacts—of masks and masking for the purposes of controlling the transmission of respiratory infection. Both lay people and healthcare workers are included.

METHODS

Search strategy

OVERVIEW OF SEARCH STRATEGY

Our initial scoping search on masks and masking in respiratory infections identified thousands of studies and more than 100 reviews. In view of this, our chosen review design is an in-depth narrative systematic review in the hermeneutic tradition, whose primary aim is to make sense of this vast literature, and within that narrative review, to include some focused meta-analyses. We seek to summarize previous reviews and also, where necessary, to analyse and critique the key primary studies on which those reviews are based. In a narrative systematic review, a thorough literature search is undertaken to identify the most influential sources in each tradition. A narrative summary is prepared based on these key sources and progressively refined by adding further sources as they are identified. This method will allow us to tease out the multiple ways in which masks and masking have been framed and examined by different groups of scientists. To identify key reviews and primary studies, we recruited authors familiar with relevant literature in a wide range of disciplines (public health, epidemiology, infectious diseases, biosecurity, fluid dynamics, materials science, modelling, data science, meta-analysis, sociology, anthropology, psychology, occupational hygiene). We began with sources known to these authors and supplemented them by searching PubMed, EMBASE and Social Science Citation Index using key words. We citation-tracked seminal sources using Google Scholar. We also sent requests to colleagues in relevant fields and posted on social media (X, Mastodon, BlueSky).

Two more specific search strategies, for the section on RCTs and the section on observational studies, are explained below.

STRATEGY FOR IDENTIFYING RCTs

In relation to RCTs, we have searched on PubMed, EMBASE, Scopus, Web of Science, and the Cochrane Library from inception. We have only included studies published in English. Search terms were: “randomised control trial”, or “randomised clinical trial”, “facemask”, or “mask”, or “surgical mask”, or “medical mask”, or “cotton/cloth mask”, or “respirator”, or “N95/N97, N99 respirator”, or “FFP2/FFP3 respirator”, or “P2/P3 respirator” or “respiratory protection”, “respiratory infections”, or “influenza”, or “influenza like illness”, or “SARS-CoV2”, or “COVID-19” or “coronavirus disease”.

STRATEGY FOR IDENTIFYING OBSERVATIONAL STUDIES

In relation to observational studies, we supplemented key studies of which we were aware through a Medline search, using terms (mask OR respirator) AND (COVID OR SARS-CoV-2 OR pandemic) AND epidemiology AND year of publication > 2019. Abstracts were reviewed to identify relevant studies for inclusion, which were supplemented with studies of which we were previously aware, including three reviews. Masking was often one component of bundled prevention strategies, so we sought to focus on studies in which mask and respirator effects could be isolated from other contemporaneous interventions. The decision to restrict observational studies to COVID-19 was made on pragmatic grounds since there was a large number of such studies.

Participant or population People wearing masks for control of respiratory outbreaks, including lay people and healthcare workers.

Intervention Wearing a mask or respirator, or being advised to wear one. Some studies with masks plus hand hygiene were included if the effects of masks could be analytical separated from the effect of hand hygiene.

Comparator Not wearing one or not being advised to.

Study designs to be included The review will cover numerous study designs, including laboratory and engineering studies, randomized controlled trials [RCTs], observational studies, mathematical modelling, surveys, communications studies, policy analyses, socio-material analyses, social media studies, and evidence syntheses of various kinds. It will examine key debates and

controversies and seek to explain why different groups of scholars take different approaches and positions.

Eligibility criteria Peer-reviewed literature will be prioritised.

Information sources Electronic databases (see details above); Sources known to the authors; Contacting experts in the field.

Main outcome(s) For the intervention studies, clinical or laboratory evidence (PCR) of influenza or other respiratory infection.

Additional outcome(s) The review seeks to make sense of a complex and contested literature, so we will be looking for explanations and debates as well as quantitative outcomes.

Data management In relation to the meta-analysis of RCTs, data extraction (selection and coding) is being undertaken as follows: Two reviewers independently extract the data from identified studies. Any differences between reviewers are reviewed by a third reviewer. The collected data are systematically recorded onto an Excel spreadsheet. A standardized extraction form is being used, encompassing various parameters such as study details (e.g., author, country of origin, year), intervention (masks, respirator or control) and primary and secondary outcomes (influenza, other viruses, CRI or ILI), total number of participants, participants with each outcome, main results, and limitations as reported by authors. In case of any discrepancies in the extracted data, a thorough re-checking and review of the primary studies is conducted to ensure accuracy. Subsequently, the compiled data are exported for meta-analysis, contributing to a comprehensive understanding of the findings across the identified studies.

Quality assessment / Risk of bias analysis To address our methodological concerns about previous RCTs (notably, the mask section of the 2023 Cochrane review on NPIs), we have separated dissimilar settings, interventions and outcome measures to conduct a meta-analysis of published RCTs. We have grouped community RCTs into “primary prevention” (masking to protect the wearer) and “source control” (masking to protect others in the community). We examined the effectiveness of masks and respirators in community and healthcare settings separately. We have excluded RCTs of “source control” and analysed only primary prevention RCTs. In community RCTs, we separately analysed RCTs of

mask and RCTs of masks plus hand hygiene. We analysed outcomes of clinical respiratory illness (CRI), influenza like illness (ILI) and laboratory (PCR) confirmed influenza and other respiratory viruses (including influenza and COVID-19).

In relation to the meta-analysis of RCTs, our strategy for data analysis is as follows. We tabulate study characteristics and perform meta-analyses using the subgroup analysis approach by outcome measures. We use the random effects model to estimate the respective pooled risk ratios (RR) and 95% confidence intervals (CI). We prepare Forest plots to show pooled estimates and corresponding 95% CIs.

Strategy of data synthesis The review team has been divided into seven sub-teams, each of whom are working largely independently on a sub-topic. The sections are: laboratory evidence, RCT evidence, observational and modelling evidence, adverse effects and harms, social and political aspects of masking, masking as policy, and environmental impact. Each team undertakes their own searches and produces a draft which is then sent to the lead author for collation. See previous responses for approach to meta-analysis specifically.

Subgroup analysis Not applicable.

Sensitivity analysis We do not plan undertake a sensitivity analysis in this review, but have highlighted key modelling studies which did.

Language restriction Papers are limited to English.

Country(ies) involved UK, Canada, USA, Australia, New Zealand, Bangladesh.

Keywords Masks, respirators, meta-analysis, social science, basic science, interdisciplinary.

Dissemination plans The review has been commissioned by a leading peer-reviewed journal. Articles for the lay press (e.g. Conversation) are planned.

Contributions of each author

Author 1 - Trisha Greenhalgh - Conceptualisation, planning and oversight of the review, searching, data extraction, interpretation, narrative synthesis. Email: trish.greenhalgh@phc.ox.ac.uk

Author 2 - Michael Baker - Lead on policy section. Study identification, data extraction, data analysis and synthesis for that section. Email: michael.baker@otago.ac.nz

Author 3 - Abrar Chughtai - Data extraction, analysis and synthesis on the meta-analysis of RCTs.

Email: abrar.chughtai@protonmail.com

Author 4 - David Fisman - Lead author on observational and modelling sections, undertaking study identification, data extraction, analysis and synthesis plus drafting that section. Revisions of full manuscript.

Email: david.fisman@gmail.com

Author 5 - Mohana Kunasekaran - Data extraction, analysis and synthesis on the meta-analysis of RCTs.

Email: mohana@epiwatch.org

Author 6 - Amanda Kvalsvig - Lived experience expert of hearing impairment. Lead on harms section. Study identification, data extraction, data analysis and synthesis for that section.

Email: amanda.kvalsvig@otago.ac.nz

Author 7 - Deborah Lupton - Lead on sociology section. Study identification, data extraction, data analysis and synthesis for that section.

Email: d.lupton@unsw.edu.au

Author 8 - C Raina MacIntyre - Lead for section on RCTs, writing methodological critique and overseeing study identification, data extraction, data analysis, synthesis, writing up. Additionally, significant contribution to conceptualisation and shaping of overall paper.

Email: r.macintyre@unsw.edu.au

Author 9 - Matt Oliver Meng - Lead for section on physical properties of masks. Identifying studies, extracting data, analysing and synthesising data.

Email: mattboliver@shaw.ca

Author 10 - Shovon Bhattacharjee - Contribution to section on environmental effects of masks and lead on section on novel materials and future designs.

Email: shovon.bhattacharjee@protonmail.com

Author 11 - Essa Tawfiq - Data extraction, analysis and synthesis on the meta-analysis of RCTs.

Email: e.tawfiq@unsw.edu.au

Author 12 - Mark Ungrin - Lead on section on evidence base for mode of transmission of respiratory infections. Study identification, data extraction, data synthesis.

Email: mark.ungrin@gmail.com

Author 13 - Joe Vipond - Contribution to section on environmental harms of disposable masks. Study identification, data extraction, data analysis.

Email: jvipondmd@gmail.com